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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,170	11/10/2000	Raymond P. Warrell	10412-025	4982

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Patrick J. Birde, Esq.  
KENYON & KENYON  
ONE BROADWAY  
NEW YORK, NY 10004

EXAMINER

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/709,170

Applicant(s)

WARRELL ET AL.

Examiner

Terra C. Gibbs

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 29-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 29-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

This Office Action is a response to Applicants Amendment and Remarks filed April 18, 2005.

Claims 1 and 19 have been amended. Claims 1-23 and 29-33 are pending in the instant application.

Claims 1-23 and 29-33 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Amendment***

Applicants Amendment to correctly identify the current status of the pending claims as required by 37 CFR 1.121 is acknowledged.

### ***Claim Rejections - 35 USC § 112***

In the previous Office Action mailed January 14, 2005, claims 1-23 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of ***treating*** cancer in a human comprising administering a bcl-2 antisense oligonucleotide at a dose of 0.01 to 50 mg/kg daily in one or more cycles of therapy, each cycle of therapy consisting of 2 to 13 days, does not reasonably provide enablement for a method of ***preventing*** cancer in a human comprising administering a

Art Unit: 1635

bcl-2 antisense oligonucleotide at a dose of 0.01 to 50 mg/kg daily in one or more cycles of therapy, each cycle of therapy consisting of 2 to 13 days. **This rejection is withdrawn** in view of Applicants amendment to the claims to delete reference to methods of preventing cancer.

### ***Claim Rejections - 35 USC § 102***

In the previous Office Action mailed January 14, 2005, claims 1-5 and 13-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Webb et al. (The Lancet, 1997 Vol. 349:1137-1141). **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed January 14, 2005.

### ***Response to Arguments***

In response to this rejection, Applicants argue that the present rejection is a reiteration, without any substantial change in logic or reasoning of the rejection dated December 15, 2003. Also, Applicants argue that the Examiner withdrew a similar rejection in the Office Action mailed July 26, 2004. Further, Applicants argue that the Examiner, in the Office Action mailed July 26, 2004, stated:

"Applicant's arguments have been fully considered and are found persuasive. The Examiner agrees that Webb teaches treating a human with one cycle of therapy for 14 days".

Applicants contend that the rejection of claims 1-5 and 13-18 must be withdrawn since the previous Office Action mailed January 14, 2005 did not present any fact or interpretation of the Webb et al. reference that Applicant has not already argued and overcome.

This argument has been fully considered but is not found persuasive because in the previous Office Action mailed April 18, 2005, the Examiner reevaluated the claims as required by 37 CFR 1.104 which discusses the nature of examination. For example, see 37 CFR 1.104 (a)(1) where it states:

“On taking up an application for examination or a patent in a reexamination proceeding, the examiner shall make a thorough study thereof and shall make a thorough investigation of the available prior art relating to the subject matter of the claimed invention”.

Further see 37 CFR 1.104 (c)(2) where it states:

“In rejecting claims for want of novelty or for obviousness, the examiner must cite the best references at his or her command. When a reference is complex or shows or describes inventions other than that claimed by the applicant, the particular part relied on must be designated as nearly as practicable. The pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified”.

In the previous Office Action mailed January 14, 2005, the Examiner followed the requirement of 37 CFR 1.104, reevaluated the claims, and clearly explained why it was her position that Webb et al anticipated the claims.

The issue at hand is the interpretation of the term “cycle of therapy”. The Examiner has defined “cycle” according to Applicant’s specification at page 7, lines 28-35 where it recites:

“cycle” refers to a period during which a single therapeutic or sequence of therapeutics is administered”.

The claims read on a method of treating cancer in a human comprising administering a bcl-2 antisense oligonucleotide in one or more cycles of therapy consisting of 2 to 13 days. Webb et al. disclose a *daily* subcutaneous infusion of a bcl-2 antisense oligonucleotide was administered for 2 weeks to nine patients (see page 1137, Methods). Webb et al. further disclose:

“one 2-week course of treatment was given. Patients were followed up for 4 weeks after the end of treatment. If there was evidence of tumor response, a second course of treatment was given” (see page 1138, second full paragraph).

Throughout prosecution, Applicants have argued that Webb teaches treating a human with one cycle of therapy for 14 days. In fact, in the Office Action mailed July 26, 2004, the Examiner agreed with this argument. However, upon the Examiner making a thorough study and investigation of the available prior art relating to the subject matter of the claimed invention as required by 37 CFR 1.104, it is the Examiner's position that Webb et al. anticipate claims 1-5 and 13-18.

It appears that Applicants are equating Webb's course of treatment with a cycle of therapy as instantly claimed. Given the broad definition of the term “cycle” in the instant specification at page 7, lines 28-35, the course of treatment disclosed by Webb et al. is not excluded from the cycle of therapy recited in the instant claims. For example, Webb et al. teach two cycles of therapy consisting of 7 days each (see Figure 2). Although at page 1137, Webb et al. recite “one 2-week course of treatment was given”, it is clear from Figure 2 that at day 7, bcl-2 levels were measured and found to be decreased. In this light, treatment/therapy was observed as early as week 1.

Although Applicants would like to argue that Webb teaches treating a human with one cycle of therapy for 14 days, the Examiner **disagrees**. The Examiner would like to point Applicant to Figure 2 where the levels of bcl-2 were measured by flow cytometry in lymph node aspirates of patient 6 during 7 days and 14 days of treatment. In fact, Webb et al. disclose, "Bcl-2 levels are reduced at weeks 1 and 2". In this example, Webb et al. clearly teach patient 6 underwent a cycle of therapy consisting of 7 days, where treatment/therapy was observed in the first week.

It is noted that a similar rejection was made in the Office Action mailed March 18, 2003. In response to this rejection, Applicants argued that Webb et al. monitored bcl-2 levels during the treatment cycle at day 7 and *monitoring* is not equivalent to Applicant's *treatment*. Further, Applicants argue that patient 6 underwent treatment for the entire 2-week period and such monitoring does not represent a shortening of the treatment period set out in the methods as instantly claimed.

If Applicants are inclined to make this argument again, it would not be found persuasive. It is clear from Figure 2 that patient 6 underwent two cycles of therapy consisting of 7 days each. Regardless of the fact that the therapy was continued for the entire 2-week period, at day 7, bcl-2 levels were measured and found to be decreased. In this regard, it is clear that at both day 7 and day 14, bcl-2 levels were decreased and therefore therapy and/or treatment was observed as early as day 7. Regarding Applicants arguments that monitoring is not equivalent to Applicant's treatment, this argument is unfounded because nowhere in Figure 2 or the text of the reference does Webb et al. mention bcl levels were *monitored*. It is clear from Figure 2 that bcl-2

Art Unit: 1635

antisense was administered to patient 6 daily for a period of 14 days. After the first week, bcl-2 levels were measured in lymph node aspirates and found to be reduced. In this light, patient 6 exhibited reduced bcl-2 levels in lymph node aspirates following administration of a bcl-2 antisense oligonucleotide. This reduction in bcl-2 was evident as early as day 7 and therefore cancer therapy was observed at week 1.

Therefore, Webb et al. anticipate claims 1-5 and 13-18.

### ***Claim Rejections - 35 USC § 103***

In the previous Office Action mailed January 14, 2005, claims 1-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al. (The Lancet, 1997 Vol. 349:1137-1141) in view of Bennett et al. [U.S. Patent No: 6,214,986]. **This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed January 14, 2005.

### ***Response to Arguments***

In response to this rejection, Applicants argue that the present rejection is a reiteration, without any substantial change in logic or reasoning of the rejection dated December 15, 2003. Also, Applicants argue that the Examiner withdrew a similar rejection in the Office Action mailed July 26, 2004. Further, Applicants argue that the Examiner, in the Office Action mailed July 26, 2004, stated:

Art Unit: 1635

"Applicant's arguments have been fully considered and are found persuasive. The Examiner agrees that Webb teaches treating a human with one cycle of therapy for 14 days".

Applicants contend that Bennett adds only motivation to experiment with dosage and administration and does not suggest the outcome of Applicants invention.

This argument has been fully considered but is not found persuasive because as discussed above, in the previous Office Action mailed April 18, 2005, the Examiner reevaluated the claims as required by 37 CFR 1.104 and made a thorough study and investigation of the available prior art. As discussed above, Webb et al. clearly teach patient 6 underwent a cycle of therapy consisting of 7 days, where treatment/therapy was observed (see Figure 2). In this light, it would have been obvious to one of ordinary skill in the art to devise a method of treating cancer in a human comprising administering a bcl-2 antisense oligonucleotide in one or more cycles of therapy, each cycle of therapy consisting of 2 to 13 days as instantly claimed.

Bennett was relied upon to teach dosage, repetition, and administration. One skilled in the art would have been motivated to administer antisense therapy further comprising administering one or more cancer therapeutics or chemoagents as taught by Bennett et al. and since it is routine and well known in the art that combination therapy is an effective approach for cancer treatment.

Therefore, the invention of claims 1-23 would have been obvious to one of ordinary skill in the art, as a whole, at the time the instant invention was made.

In the previous Office Action mailed January 14, 2005, claims 29-33 were rejected under 35 U.S.C. 103(a) as being unpatentable over Webb et al., (The Lancet, 1997 Vol. 349:1137-1141) in view of Bennett et al. [U.S. Patent No: 6,214,986]. **It is noted that Applicants response filed April 18, 2005 failed to provide remarks or arguments regarding this rejection. This rejection is maintained** for the reasons of record set forth in the previous Office Action mailed January 14, 2005.

Applicant's amendment necessitated the new ground(s) of rejection presented below:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "in which such treatment or prevention" in line 3. There is insufficient antecedent basis for this limitation in the claim because the claim has been amended to delete reference to methods of preventing cancer.

Claim 19 recites the limitation "in which such treatment or prevention" in line 2. There is insufficient antecedent basis for this limitation in the claim because the claim has been amended to delete reference to methods of preventing cancer.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wang Andrew can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg  
June 28, 2005



**ANDREW WANG**  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600